REMARKS

Claims 1-61 were pending. In the Office Action, the Examiner indicates that claims 6, 11-14, 21, 24-48, 56, and 57 are withdrawn. Applicants respectfully submit that claim 28 is not withdrawn by the restriction requirement/election of species dated October 3, 2007. Claim 28 is directed to an implantable device which further comprises an antioxidant encapsulated within said matrix. Claim 28 is part of elected Group I, and the subject matter of antioxidants were not subject to election of species in the Office Action dated August 3, 2007. As claim 28 reads on an elected group/species, the Examiner is requested to remove the "withdrawn" status as indicated in the present Office Action for this claim.

By virtue of this response, new claims 62-87 have been added, claims 1, 10, 16, 49, 51, and 58 have been amended, and claims 8 and 23 have been canceled. Claims 1, 16, and 49 are amended to clarify that a dopamine agonist binds to one or more dopamine receptor subgroups. Claims 1 and 49 are amended to clarify that implantable device, when implanted subcutaneously in a mammal, results in a steady state plasma level of at least about 0.01 ng/ml for the sustained period of time. Claims 1, 16, and 49 are amended to include the limitation: wherein the implantable device is produced by an extrusion process, and wherein the implantable device is uncoated. Claims 8 and 23 have been canceled as redundant in light of the amendments to claims 1 and 16. Claim 10 is amended for clarification. Claims 51 and 58 are amended to correct typographical errors. Support for the new and amended claims may be found throughout the specification and claims as originally filed, for example at, *inter alia*, paragraphs [0018], [0021], [0025], [0031]-[0032], [0034], and [0051] of the application. No new matter is believed to be introduced by these new claims and amendments.

Accordingly, upon entry of this amendment the Applicants believe that claims 1-87 are pending, with claims 6, 11-14, 21, 24-27, 29-48, 56, and 57 withdrawn. The Examiner is respectfully requested to reconsider and verify the pending and withdrawn claim status in the next action.

The Applicants note that upon allowance of a generic claim, Applicants will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of allowed generic claims as provided by 37 C.F.R. § 1.141.

With respect to all amendments and cancelled claims, Applicants have not dedicated or abandoned any unclaimed subject matter and, moreover, have not acquiesced to any rejections and/or objections made by the Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation, continuation-in-part, and/or divisional applications.

Rejections under 35 U.S.C. § 102

Claims 1-4, 7-10, 15-19, and 22-23 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Sabel et al., "Extended Levodopa Release from a Subcutaneously Implanted Polymer Matrix in Rats." The Examiner asserts the rejection of claims 3, 15, and 18 is evidenced by Freese et al., "Controlled Release of Dopamine from Polymeric Brain Implant: *In Vitro* Characterization", and the Elvax® Specialty EVA Resins disclosures ("Elvax"). The Applicants respectfully traverse this rejection.

Sabel relates to a slow-release polymer matrix system that can deliver levodopa. Freese relates to a biocompatible polymeric matrix system for the long-term controlled release of dopamine directly into the brain.

Neither Sabel nor Freese teach an implantable device that is extruded, as required by amended independent claims 1 and 16, and therefore dependent claims 2-4, 7-10, 15, 17-19 and 22-23. Rather, Sabel as shown by Freese discloses an implant comprising levadopa which is formed by solvent casting and is subsequently coated. Freese discloses dopamine-containing implants which are formed by solvent casting.

Further, neither Sabel nor Freese teach an implantable device that is extruded and uncoated, wherein when said implantable device is implanted subcutaneously in said mammal, said

dopamine agonist is continuously released *in vivo* over a sustained period of time through pores that open to the surface of said matrix at a rate that results in a steady state plasma level of at least about 0.01 ng/ml for the sustained period of time, as required by claim 1, and therefore dependent claims 2-4, 7-10, and 15. Sabel and Freese also do not teach an implantable device that is extruded and uncoated, wherein when said implantable device is subcutaneously implanted in a mammal, said dopamine agonist is continuously released *in vivo* over a sustained period of time through pores that open to the surface of said matrix at a rate of at least about 0.1 mg of dopamine agonist per day at steady state, as required by claim 16, and therefore dependent claims 17-19 and 22-23. The *in vivo* plasma level of levadopa reported in Sabel is highly variable; Figure 2B on page 716 indicates that the plasma level of levadopa varies from about 112 ng/ml at about 35 days post-implantation to about 12 ng/ml at about 225 days post-implantation. Freese does not disclose *in vivo* plasma levels obtained from subcutaneous implantation of the disclosed uncoated devices. However, Figure 1A on page 235 indicates that *in vitro* release of dopamine from the uncoated, solvent-extruded device is very rapid.

Additionally, Sabel and Freese do not disclose an implantable device comprising dimensions of about 2 to about 3 mm in diameter and about 2 to about 3 cm in length, as required by claim 9. Rather, Sabel discloses a device that is 15 x 30 x 2 mm. Freese discloses devices that are round discs 4.0 mm in diameter and 1.0 mm in depth.

Accordingly, Applicants respectfully request that the Examiner withdraw the rejection under 35 U.S.C. § 102(b).

Rejections under 35 U.S.C. § 103(a)

A. Claims 49-55 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Sabel et al. The Applicants respectfully traverse this rejection.

Sabel relates to a slow-release polymer matrix system that can deliver levodopa. As an initial matter, Applicants note that levadopa is not a dopamine agonist that binds to one or more dopamine receptor subgroups. Levadopa is a precursor to dopamine, and therefore does not bind

directly to dopamine receptors: "*Levadopa is itself largely inert*, its therapeutic as well as adverse effects result from the decarboxylation of levadopa to dopamine [emphasis added]." (Standaert DG, Young AB. Treatment of central nervous system degenerative disorders. In: Hardman JG, Limbird LE, Eds., *Goodman and Gilman's The Pharmacological Basis of Therapeutics*, 10th Ed., New York, NY, McGraw-Hill, 2001, pp. 555. A copy of this document is enclosed herewith for the Examiner's convenience). Although Sabel hypothesizes that peripheral implantation of polymer matrices containing dopamine receptor agonists *might* comprise a useful method, Sabel teaches that levadopa is preferred: "Numerous investigators have now shown that continuous delivery of L-Dopa constitutes the best mode of treatment for parkinsonian patients." (page 716). Thus, Sabel developed a system for levadopa treatment rather than treatment with a dopamine agonist. Sabel gives no teaching about plasma levels of dopamine agonists that are therapeutically beneficial for treating diseases such as Parkinson's.

Sabel does not teach or suggest an implantable device comprising a dopamine agonist that binds to one or more dopamine receptor subgroups, wherein the implantable device is produced by an extrusion process, wherein the implantable device is uncoated, and wherein when said implantable device is implanted subcutaneously in said mammal, said dopamine agonist is continuously released *in vivo* over a sustained period of time through pores that open to the surface of said matrix at a rate that results in a steady state plasma level of at least about 0.01 ng/ml for the sustained period of time. Sabel thus does not teach or suggest a kit comprising at least one implantable device comprising a dopamine agonist that binds to one or more dopamine receptor subgroups, wherein said at least one implantable device is produced by an extrusion process, wherein said at least one implantable device is uncoated, and wherein when said at least one implantable device is implanted subcutaneously in a mammal, said dopamine agonist is continuously released *in vivo* from each of said at least one implantable devices over a sustained period of time through pores that open to the surface of said matrix at a rate that results in a steady state plasma level of at least about 0.01 ng/ml for the sustained period of time and instructions for use in a method of administration of a dopamine agonist to a mammal in need thereof, as required by independent claim 49 and dependent claims 50-55.

B. Claims 5, 20, 59-61 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Sabel et al. in view of Edgren (U.S. 5,128,145). The Applicants respectfully traverse this rejection.

As noted by the Examiner, Sabel lacks a teaching of lisuride. Edgren merely provides a listing of anti-Parkinson's drugs, and does not teach the equivalency of lisuride and levadopa. Further, Edgren does not teach that both are ergot derivatives, but rather that lisuride, pergolide, and mesulergine are ergot derivatives: "an anti-Parkinson drug selected from…ergot derivatives including lisuride, pergolide, and mesulergine; levadopa; carbidopa;…[punctuation emphasis added]"

Sabel does not teach or suggest an implantable device comprising a dopamine agonist that binds to one or more dopamine receptor subgroups, wherein the implantable device is produced by an extrusion process, wherein the implantable device is uncoated, and wherein when said implantable device is implanted subcutaneously in said mammal, said dopamine agonist is continuously released *in vivo* over a sustained period of time through pores that open to the surface of said matrix at a rate that results in a steady state plasma level of at least about 0.01 ng/ml for the sustained period of time, as required by claims 5, 59, and 61. Additionally, Sabel does not teach or suggest an implantable device comprising a dopamine agonist that binds to one or more dopamine receptor subgroups, wherein the implantable device is produced by an extrusion process, wherein the implantable device is uncoated, and wherein when said implantable device is subcutaneously implanted in a mammal, said dopamine agonist is continuously released *in vivo* over a sustained period of time through pores that open to the surface of said matrix at a rate of at least about 0.1 mg of dopamine agonist per day at steady state, as required by claims 20 and 60.

Alone or in combination with Edgren, Sabel fails to teach or suggest an implantable device comprising a dopamine agonist that binds to one or more dopamine receptor subgroups, wherein said dopamine agonist is lisuride, wherein the implantable device is produced by an extrusion process, wherein the implantable device is uncoated, and wherein when said implantable device is implanted subcutaneously in said mammal, said dopamine agonist is continuously released

in vivo over a sustained period of time through pores that open to the surface of said matrix at a rate that results in a steady state plasma level of at least about 0.01 ng/ml for the sustained period of time, as required by claims 5, 59, and 61. Additionally, Sabel, alone or in combination with Edgren, does not teach or suggest an implantable device comprising a dopamine agonist that binds to one or more dopamine receptor subgroups, wherein said dopamine agonist is lisuride, wherein the implantable device is produced by an extrusion process, wherein the implantable device is uncoated, and wherein when said implantable device is subcutaneously implanted in a mammal, said dopamine agonist is continuously released *in vivo* over a sustained period of time through pores that open to the surface of said matrix at a rate of at least about 0.1 mg of dopamine agonist per day at steady state, as required by claims 20 and 60.

C. Claim 58 is rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Sabel et al. in view of WO 98/20864 ("'864"). The Applicants respectfully traverse this rejection.

'864 relates to the use of selected non-steroidal anti-inflammatory compounds for the prevention and the treatment of neurogenerative diseases.

As discussed above, Sabel does not teach or suggest a kit comprising at least one implantable device comprising a dopamine agonist that binds to one or more dopamine receptor subgroups, wherein said at least one implantable device is produced by an extrusion process, wherein said at least one implantable device is uncoated, and wherein when said at least one implantable device is implanted subcutaneously in a mammal, said dopamine agonist is continuously released *in vivo* from each of said at least one implantable devices over a sustained period of time through pores that open to the surface of said matrix at a rate that results in a steady state plasma level of at least about 0.01 ng/ml for the sustained period of time and instructions for use in a method of administration of a dopamine agonist to a mammal in need thereof, as required by independent claim 49, and therefore dependent claim 58.

Alone or in combination with '864, Sabel fails to teach or suggest a kit comprising at least one implantable device comprising a dopamine agonist that binds to one or more dopamine

receptor subgroups, wherein said at least one implantable device is produced by an extrusion process, wherein said at least one implantable device is uncoated, and wherein when said at least one implantable device is implanted subcutaneously in a mammal, said dopamine agonist is continuously released *in vivo* from each of said at least one implantable devices over a sustained period of time through pores that open to the surface of said matrix at a rate that results in a steady state plasma level of at least about 0.01 ng/ml for the sustained period of time and instructions for use in a method of administration of a dopamine agonist to a mammal in need thereof, wherein the at least one implantable device further comprises an anti-inflammatory agent, and said anti-inflammatory agent is encapsulated within a biocompatible, nonerodible polymeric matrix that does not comprise said dopamine agonist, as claimed in claim 58.

In view of the above remarks and amendments, the Applicants assert that the presently pending claims are not obvious and request withdrawal of the above-listed rejections (**A-C**) under 35 U.S.C. § 103(a).

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to ***Deposit Account No. 03-1952*** referencing docket no. **304142000900**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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